T.& B. Vol. 22. p. 40.

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REPRINT FROM
THE SOUTHERN MEDICAL JOURNAL
Journal of the Southern Medical Association
Birmingham, Alabama
Vol. XVII August 1924 No. 8
Pages 590-596

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THE SPLEEN INDEX IN MALARIA*

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Notwithstanding the wide use of the spleen index in the Orient as a measure of malaria, the method has not met with general acceptance in the Southern states by the men who are making malarial surveys, and by those who are concerned in measuring malaria before and after the inauguration of control measures. In the Orient there is of course the language difficulty when working with natives, and this is an additional reason for having an objective method which will yield trustworthy results without having to rely on the testimony of ignorant, suspicious, overconciliatory or uncooperative persons.

Those concerned in malaria control must have some method for measuring malaria. Histories, under the circumstances, are subject to considerable error. All native, subject, or dependent people are inclined to give the information which they believe the interrogator wishes to know. This is particularly true among negroes everywhere. Suspicious persons will deny that they have had the disease for fear that it is desired to sell them something. There is the difficulty of interpreting the statements of the persons. "Fever" may mean the fever associated with colds or it may, and frequently does, mean the spells of debility experienced by persons living in a warm climate. Again, even in heavily infected households, some members will give a straightforward

*Read before the National Malaria Committee (Conference on Malaria), meeting conjointly with Southern Medical Association, Seventeenth Annual Meeting, Washington, D. C., Nov. 12-15, 1923.

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history of chills and fever, while others whose blood may be positive at the time of the examination complain of headache and fever, or merely headache. Some persons may deny having any symptom of malaria, although their blood contains notable numbers of plasmodia. This is particularly true of native people long exposed to the debilitating effects of malaria.

In view of the difficulty of eliciting histories which may be relied upon, is it possible to gain the information desired by some other, preferably objective, method?

Malaria is not a disease which may be measured easily and accurately, for the reason that except when the plasmodia are present in the peripheral blood they secrete themselves in the recesses of the spleen and bone marrow where it is often impossible to detect their presence.

Manson long ago pointed out that malaria is a disease in which the phenomena in the peripheral blood represent merely an overflow while the tragedy is being played in the inner viscera. The overflow may be detected by an examination of the peripheral blood. When there has been segregation of parasites in the placenta they may be detected in that organ after delivery, as Clarke has pointed out. The marrow is not usually subject to examination nor is the spleen, but the latter organ undergoes enlargement during the infection and may remain enlarged for several weeks after the infection has subsided in the peripheral circulation. It is this organ which really shows the extent of the big "visceral happenings" in malarial infection.

Sydenham* had noted the relation of ague to swelling of the spleen, for he says:

"It is worth observing that when these autumnal agues have for a long time afflicted children, there is no hope of dispelling them until the abdominal region, especially in the neighborhood of the spleen, has begun to swell and harden, whilst in proportion as this symptom increases the ague goes off. Perhaps there is no better symptom

*Sydenham: The Works of Sydenham, Vol. 1, Medical Observations; chapter v, p. 50, Latham's Translation of Greenhill's Latin edition made for the Sydenham Society, London, mdcccxlviii.

whereon we may form a favorable prognosis as to speedy termination of the disease than the one in question. Observe it watchfully."

The English in India have been familiar with the association of splenic enlargement and malaria for many years. The earliest observation seems to have been made by Dempster. Later workers have used the spleen in measuring the amounts of malaria in different circumstances of age, race, geographical region and locality and as affected by season, rainfall, etc.

The most distinguished and experienced malarial epidemiologists who have worked in the Orient, for example, Ross, Christophers, James, Watson, Schuffner and Swellengrebel, are convinced of its great value. The method was used by the Uncinariasis Commission to the Orient in their efforts to measure malaria in the Malay Peninsula and Java.

At the Fourth Congress of the Far Eastern Association of Tropical Medicine assembled in 1921, a Committee was appointed to determine the most usable means of employing the spleen rate, rapidly and accurately, so convinced are they that it is a "precious asset" of the malariologist. Barber, Coogle and Maxcy have more recently used in the South a method of estimating the amount of malaria by ascertaining the proportion of school boys who had enlarged spleens.

Malaria is a constantly moving problem whether we contemplate the disease in an individual, in a community or in the infected mosquitoes which carry it from one person to another. Hence, it is not to be supposed that we can get a clear picture of the disease at rest, or that the rates or indices exist for longer than a short period of time. The cross section is constantly changing. In a large group of prisoners, which I studied in the Netherlands Indies, it was interesting to note the flux of relations within the group. The men were exposed to malaria night after night without any screening protection whatever. Spleen rates and blood rates were ascertained on several successive occasions. It was noted that the bloods of the prisoners became positive and then declined. Spleens en-

larged to enormous size and later diminished in bulk. Hemoglobins in similar manner waxed and waned as the infection came under control as a result of the activity of the bodily mechanism of defense. It was remarkable that the prisoners as a whole who furnished the rates and who were constantly present in the jail yielded the same rates on the various occasions they were examined, but the individuals whose blood happened to be infected at the time of examination, or the person whose spleen happened to be enlarged, were not the same on each occasion. While the rate for the entire jail remained the same, the actual spleens and positive bloods were not the same. It is important to remember this because we must bear in mind that rates and indices and reports of positive and negative blood are only relative statements. Persons once infected with malaria may remain infected for years. These persons furnish the cases of malarial relapse. A person whose blood becomes negative should not be regarded as actually free from malaria. A negative report of a blood film means merely that no plasmodia were found during the time spent by the examiner on that particular film. A larger amount of blood might more readily show plasmodia. A negative blood or spleen does not preclude the presence in the individual of malarial infection.

THE RELATION OF MALARIA TO ENLARGED SPLEEN

Opportunity was obtained in the Orient to ascertain the manner in which splenic enlargement occurred in new infections and in relapse. Anophelines were experimentally infected with subtertian malaria and later the infection was induced experimentally in two men. After an incubation period during which the spleen could not be palpated, the patients became ill and at the same time the spleen became palpable and plasmodia appeared in the blood. After plasmodia had disappeared from the peripheral blood the spleen in one case remained enlarged for several weeks. The splenic reaction was more marked in the case that had had malaria previously.

The behavior of the spleen in relapse was observed in patients who were under observation

in our wards and under treatment for hookworm infection. It was noted that when a relapse occurred the spleen, which had been perhaps of normal palpability previous to the relapse, became enlarged. After parasites had disappeared from the peripheral blood the spleen slowly returned to normal or to nearly its normal size.

The cause of the splenic enlargement is probably to be sought in the causes which lead to the segregation of defunct and infected erythrocytes there, and to the phagocytosis of malarial pigment by splenic endothelium. There is an interesting correspondence between the appearance of plasmodia, the enlargement of the spleen, the diminution of hemoglobin and the reduction in the number of erythrocytes in the blood. As the spleen diminishes in size after the access of fever there is an improvement in the blood picture. The hemoglobin and the blood cells increase to normal numbers.

The enlargement of the spleen is due, then, in the first instance to the malarial infection and to the increased volume of injured and infected erythrocytes and pigment in that organ. Since the spleen enlarges during the attack and remains enlarged for some time afterward, the organ should be an important means of diagnosis of the infection when, as is often the case, the plasmodia have disappeared from the peripheral blood and have retired to the spleen and marrow. It is questionable whether the spleen does not become a more important means of diagnosis of malarial infection present and recently acquired than the blood picture and presence of plasmodia, for the enlargement of the spleen indicates the presence of plasmodia in the deeper viscera when they are not demonstrable by an examination of the peripheral blood.

The spleen may enlarge to enormous proportions in regions where the endemicity is high. Malariologists have been accustomed to using a rough estimate of the volume of the spleen as being palpable or enlarged to 1, 2 or 3 finger breadths below the costal margin, or even four finger breadths, or to the umbilicus or pelvis.

These very large spleens are encountered among people who are underfed and habitually subsist on an insufficient ration. Their resistance is too low to enable them to reduce the infection promptly or properly. The classification of the spleen according to the different degrees of enlargement has a basis in the fact that there is a greater degree of malaria in the spleens of large size. In the Orient, where there exists an enormous population subsisting on an insufficient and unbalanced ration, where large masses of the population are habitually underfed, malaria produces, in conjunction with underfeeding, spleens of very large size. Oriental malariologists are so accustomed to these large spleens that they use coarse methods of measuring the degrees of enlargement in malaria.

In the Southern states, where there is less underfeeding and where those infected with malaria subsist on a more nearly balanced ration than Oriental people, the larger spleens will be less frequently encountered. Probably finer methods of detecting the degrees of splenic enlargement or a more delicate scale will have to be used in the South.

In spite of the extensive use of the spleen census in estimating malaria little has been written on the rationale of the subject, nor have investigations been conducted to ascertain the limits of usefulness of the method.

It is to the latter subject that I have been led in my inquiries into malaria in Lee County, Georgia, where the International Health Board has established a laboratory to study certain field problems in malaria. The investigation is not completed and an analysis has not yet been made of all the data collected, but some of the more interesting points that have emerged may be mentioned at this time.

The following classes of spleens are being tentatively used at the present time at our station:

(1) Negative on deep inspiration.

(2) Palpable on deep inspiration.

(3) Palpable on normal inspiration, but not 1 finger's breadth below the costal margin.

(4) One finger's breadth below the costal margin in normal respiration.

(5) Two fingers breadth below the costal margin in normal respiration.

(6) Three or more fingers breadth below the costal margin in normal respiration.

The Relation Between Degree of Splenic Enlargement and Malarial Infection.—A definite relationship exists between the size of the spleen and the amount of malaria as measured by the presence of plasmodia in the peripheral blood, and the spleens of the higher degree of enlargement are positively correlated with the presence of plasmodia in the peripheral blood.

It is seen that persons with spleens enlarged to the higher degree are more apt to have plasmodia in the peripheral blood than others, but it is to be noted that spleens of all degrees of enlargement are malarial, and the larger the spleen the more likely its possessor is to have plasmodia in his peripheral blood. Even the spleen that is only palpable on inspiration is as good as index of malaria as the spleen just palpable below the costal margin.

The spleen just palpable on deep inspiration is encountered in the winter after the malaria in the community and in the individual has subsided and it is found on plantations where the malaria is very light. It is, then, an indication of light or residual malaria.

Method of Examination.—In order to elicit these smaller degrees of enlargement and better to determine the exact degree of enlargement of any spleen, it is necessary to place the child in a recumbent position with the thighs and legs flexed. The clothing is loosened so that the hand of the examiner can be placed upon the bare skin of the abdomen in the region of the spleen, above and below the costal margin. The child is instructed to take a deep breath. With the tips of the fingers of the right hand held at and just below the costal margin, slight pressure is made as the child takes a deep breath. Then if the spleen is enlarged it may be felt as it descends, being pushed down by the diaphragm.

Care must be taken not to press too deeply or the border of the spleen may be missed.

Spleens that are palpable or of the higher degrees of enlargement may be palpated without the necessity of the child's taking a deep breath, although, for the examiner to make a uniform comparison of all the spleens, it is necessary to have the child breathe deeply in every case.

The Class of Children to Include in the Spleen Index.—The spleen may be palpated more easily in children between the years of 2 and 12 than those younger or older. For this reason and for the equally important one that children, after the age of puberty, who have always lived in an endemic region, are less apt to have enlarged spleens than the younger ones, it is advisable to limit the children examined to those between the ages of 2 and 12.

It is the practice at our station in Lee County, Georgia, to examine the negro boys and girls at the school or preferably at the quarters on the plantation. At the latter place the smaller children can be found and the parents can be questioned and advised when we encounter cases that urgently require treatment. The plantation is the location of preference for another reason. Malaria is a local problem and, at the time the spleen rate is determined on the plantation, all the houses are searched for anopheline mosquitoes, which are dissected later to determine the sporozoite rate. The neighborhood within flight distance is also searched for breeding places. Thus a complete picture of the malarial environment is obtained. Malarial rates are therefore referred to the locality and not to a county or township or school. It is obviously more important to refer the rate to the actual locality than to merge it with others of a different type of locality having a different problem for control. White children are taken at the homes or the school, but the spleen examination of girls is conducted at their homes and not at the school. Perfect cooperation has been a rule. Negro parents have often washed their children and sent them to us cleanly and freshly dressed for examination. White mothers have brought their girls

to homes where we have been engaged in examining the girls of other parents.

The Spleen Rates Found in Lee County, Georgia.—It is possible to analyze the rates obtained from some 30 plantations in Lee County, Georgia, and compare the spleen rates with the history rates and these with the endemic index or parasite rate. There are 571 histories which it is possible to analyze in this way.

Total cases with histories either positive or negative for malaria	571
Percentage of these giving a positive malarial history	37.4
Percentage with positive or enlarged spleen	40.8
Percentage with positive bloods	25.2

By the method employed it is seen that the spleen rate corresponds closely with the percentage of cases giving a positive history of malaria since the beginning of the year.

Twenty-one plantations yielded spleen rates from 15 to 89, while the endemic index or parasite rate of these same plantations ranged from 7 to 54. These rates were, for the most part, obtained during the spring and summer before the malaria had reached its height. In the re-examination now underway even higher rates are being found. As was pointed out above, most of these enlarged spleens are of the smaller degree of enlargement, although many were one finger's breadth below the costal margin on deep inspiration, which is definitely a pathological spleen. The number of spleens which were palpable on inspiration or merely palpable was 177 out of 592 examined, a proportion equal to 29.3 per cent. The spleens of a larger size or those one finger breadth and larger are 82 in number, or equal to a rate of 13.8 of the whole number of cases examined. The average spleen rate of these 21 plantations is 55.4, while the endemic index or

DEGREE OF SPLENIC ENLARGEMENT

	Negative Spleen	Palpable on Inspiration	Palpable	1 Finger Breadth	2 Fingers Breadth	3 Fingers Breadth
Per cent with plasmodia in the peripheral blood	11.2	35.3	34.1	55.1	60.0	69.5
Total cases in group	338	51	126	29	30	23

parasite rate is 31.8. Taking the entire number, if the spleen rate is multiplied by the factor 0.57, it will yield the parasite rate. It would be possible, therefore, to derive a parasite rate from a spleen rate without the examination of blood when large numbers are taken. But, as we have already pointed out, the control of malaria is a local question and the rates should be referred to the locality and not to a larger artificial geographical unit. The spleen rate of the negro children of Lee County is about 40, but this does not give a fair idea of the distribution of the disease which is generally severe, though patchy, some plantations having a low rate and others very high.

DISCUSSION AND SUMMARY

A method of estimating malaria which is used so extensively by distinguished authorities in the Orient must possess a usefulness in the Southern states if measurable malaria exists in the latter region.

Malaria is a disease the phenomena of which take place not only in the peripheral blood, but, to a greater and more prolonged extent, in the internal viscera, notably the spleen.

Among the negro children examined in Lee County, Georgia, there is a measurable correspondence between the degree of splenic enlargement and the amount of malaria as measured by the occurrence of plasmodia in the peripheral blood. That is to say, the larger the spleen the more apt is one to find plasmodia in the peripheral blood.

All degrees of enlargement are indicative of malaria. Even the smaller spleens show more evidence of the presence of malaria than the spleens which are entirely negative upon the most careful examination. The examination can be carried out on the children between the ages of 2 and 12 wherever it is convenient, at the plantation or school, but in each instance the spleens should be referred back to the locality of origin by ascertaining the residence of the subject. In this way the spleen rate becomes an accurate reflection of the amount of malaria in the immediate environment of the children examined.

The time required to ascertain the spleen rate is very much less than that required for history taking and for taking blood specimens and the results are obtained immediately without the necessity of waiting for the examination of the blood specimens.

When the spleens are classified and the results of the census are expressed in terms of spleens of different sizes, there may be less diagnostic error involved than when either histories or blood examinations are used. The more refined the method for detecting even the smaller degrees of enlargement the more accurately may the amount of malaria be determined. This is of course true then the most accurate method will have to be of any clinical method. If it is desired to ascertain with great accuracy the amount of malaria, what degree of accuracy they will need for their used. Epidemiologists will have to determine purposes.

At the present time the results of different observers will show certain discrepancies although they agree as to the general prevalence of malaria. Malariologists in the Orient encounter many examples of greatly enlarged spleens in the undernourished and severely infected natives of those regions, and they use methods which are too coarse to detect the finer degrees of enlargement to be found in regions such as the South, where there is less underfeeding and generally less severe malaria than in the Eastern countries.

From the observations taken so far in Lee County, Georgia, it can be stated that the spleen index appears to afford a very sensitive, accurate and easily applied method of detecting present and recently acquired malaria. It will detect the cases of malaria acquired the previous season, which furnish the chronic carriers of the disease, in which the blood is sometimes negative. It is these carriers which infect Anophelines in the following spring and summer and give rise to epidemics or to seasonal endemicity. The spleen census rests on a malarial basis, and because of the larger numbers involved will probably furnish a more sensitive measurement of malaria than the blood index. Its accuracy and trustworthiness

depend upon the examiner and not upon the testimony of an ignorant, careless or otherwise unsatisfactory subject. For this reason it may become the method of preference over that of the clinical history or of blood examination, which latter mode is more objectionable to children and the most difficult to carry out.

DISCUSSION

Dr. K. F. Maxcy, U. S. Public Health Service, Montgomery, Ala.—Two years ago the United States Public Health Service undertook to make investigations along this line. Dr. Darling's work has been intensive and qualitative, while ours has been extensive and quantitative. We wanted to find out, in the first place, if the spleen rate could be applied in different parts of the United States, and, in the second place, if it could be used as an index of the amount of malaria present.

It makes a great difference at what time of the year the examinations are made. For reasons which are obvious we chose the winter months. The period of transmission in the United States is considerably shorter than in the tropics. Outside of July, August and September there is little transmission going on. During the winter months we should expect less variation in the spleen rates than during the summer months. This consideration is particularly significant in dealing with so small a unit as a plantation. For instance, you might visit a plantation just before an outbreak of malaria, or during one, and obtain widely different spleen rates.

We chose the school unit because of its practical availability. It has its drawbacks, but also has its advantages, one of which is that the school unit is present everywhere, while the plantation unit is not. In large parts of the South the plantation system is no longer in existence.

The disadvantage is that the school may draw from a fairly large area, particularly if it be a consolidated school. There may be one particular locality in this school district which is heavily infected with malaria, while the remainder of the district is relatively free. In such a case, the per cent of positive spleens seems small, being diluted by the negatives from the malaria-free neighborhoods. The per cent of enlarged spleens in a school group may be low, therefore, in the presence of a small, badly infected neighborhood.

The third point was the question of whether we should include the girls along with the boys. Inasmuch as the method is simply an index, and we are selecting a population group anyway, and since we have, at present, no information as to any difference between male and female as regards the incidence of malaria, we chose boys of school age as our population group.

The fourth point was whether the children should be examined in dorsal decubitus, or standing. Because of practical advantages under field conditions, we decided to use the standing position. The patient was bent slightly forward, with the abdominal muscles relaxed, breathing deeply, and the palpating hand was next to the skin, for routine. We checked doubtful results by a subsequent examination with the patient lying down. It is our impression, from a rather large experience, that we do not miss many of the definitely palpable spleens on account of the method when once skill has been attained in using it. Both methods are used by tropical workers and their relative reliability is a mooted question.

Another question was this: if we are going to use spleen rates to determine malaria, we want to make the results as nearly comparable everywhere as possible. We want to use a method that requires ordinary skill and not a method that requires excessive skill; one that could be used by any county health officer. In other words, if there is any variation in results when two individuals go over a group of spleens, it is in the barely palpable spleens which one man can feel and the other cannot. For that reason we decided to record only the spleens palpable beyond all question of doubt. The results we have obtained so far should be considered in the light of that point of view and that method.

The work already done has shown conclusively that in certain areas in the United States where malaria is highly prevalent the spleen rate of school boys taken during the winter months is sufficiently high to be of value in an index. In other areas, lightly infected with malaria, this does not hold true. It is impossible to predict what will be found. The experience gained in one area may be contradicted by the findings in another, apparently similar. For example, we were very much surprised to find a spleen rate of about 3 per cent in a group of 212 children on the plantations at Mound, La., when the parasite index was close to 12 per cent, while a group of

426 colored boys in the Mississippi Delta, taken from January to April, 1923, showed a spleen rate of 13 per cent and a parasite rate of only 6 per cent.

It is not unlikely that the local demand for quinin and quinin containing nostrums in this country is responsible for differences in the spleen rate, as has been suggested many times before. That our rates are considerably lower than those found in tropical countries is also not strange in view of the fact that in the southern United States the period of active transmission of malaria is only three to four months and the infected persons have eight or nine months in which to recover, whereas in many tropical countries it lasts throughout the greater portion of the year and the population has little respite from new infections. There are many other factors which differ.

However, the fact remains that the spleen rate is sufficiently high in many parts of the southern United States to be valuable as an index and it should be utilized more than it has been in the past.

Dr. Darling (*closing*).—These figures are based on negro children, a large number of whom had taken a little quinin in the form of chill tonic, but in insufficient quantity to affect the disease.

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